Claims

1. An expression vector comprising DNA encoding a subunit of a dimeric form of interleukin under transcriptional control of an ecdysone-inducible promoter.

2. A vector as claimed in Claim 1 in which the subunit of a dimeric form of interleukin is selected from the group comprising: p35 (alpha) subunit of interleukin 12 (IL-12); p40 (beta) subunit of IL-12; p19 chain of IL-23; p40 subunit of IL-23; ebi3 subunit of IL-27; and p28 subunit of Il-27.

3. A vector as claimed in Claim 1 or 2 comprising an ecdysone-inducible mammalian expression plasmid, wherein the DNA encoding the subunit of a dimeric form of interleukin is included in the plasmid.

4. A vector as claimed in any preceding Claim in which the DNA encodes a p40 subunit of IL-12.

5. A vector as claimed in any of Claims 1 to 3 in which the DNA encodes a p35 subunit of IL-12.

6. A vector as claimed in any of Claims 1 to 3 in which the DNA encodes a p19 subunit of IL-23.

7. An expression vector as claimed in Claim 1 or 6 in which the ecdysone inducible mammalian expression vector is selected from the group comprising: pIND; pIND(SP1); and pINDHygro.

8. An expression vector as claimed in any of Claims 1 to 7 in which the DNA encoding a subunit of dimeric interleukin 12 includes a DNA sequence encoding a 6 x histidine tag.

9. An expression vector as claimed in any preceding Claim selected from the group comprising: pIND-p35H; pIND(SP1)-p35H; pIND-40H; pINDHygro-p40; pIND(SP1)-p40H; and pIND-p40.

10. An expression vector as claimed in any preceding Claim in which the DNA encoding the subunit of dimeric interleukin is digested with NheI and XhoI restriction enzymes prior to ligation of the digested DNA products into the expression vector.

11. The expression vector pIND(SP1)-p35H having ECACC accession number 03120401.

12. A method a producing a tightly controlled expression vector capable of transforming a host cell which when transformed is capable of producing a

recombinant dimeric interleukin, or a subunit thereof, under transcriptional control of an ecdysone-inducible promoter, comprising the steps of:

- providing cDNA for a subunits of a dimeric interleukin;
- digesting the cDNA with at least one restriction enzyme; and
- ligating the digested cDNA product into an ecdysone-inducible mammalian expression vector.

13. A method as claimed in Claim 12 in which the one or more restriction enzymes consist of *NheI* and *XhoI*.

14. A method as claimed in Claim 12 or 13 in which the ecdysone-inducible mammalian expression vector is selected from the group comprising: pIND; pIND(SP1); and pINDHygro.

15. A method as claimed in any of Claims 12 to 14 in which the cDNA for the subunit of dimeric interleukin includes a DNA sequence encoding a 6 x histidine tag.

16. An expression vector obtainable by the method of any of Claims 12 to 15.

17. A cell line transfected with at least one expression vector of any of Claims 1 to 11 or 16, wherein the DNA encoding the at least one subunit of

a dimeric interleukin is under the transcriptional control of an ecdysone-inducible mammalian expression system.

18. A cell line according to Claim 17 and capable of producing homodimeric IL-12, the cell line being transfected with an expression vector of Claim 4.

19. A cell line according to Claim 17 and capable of producing heterodimeric IL-12, the cell line being transfected with an expression vector of Claim 4 and an expression vector of Claim 5.

20. A cell line according to Claim 17 and capable of producing heterodimeric IL-23, the cell line being transfected with an expression vector of Claim 4 and an expression vector of Claim 6.

21. A cell line of any of Claims 17 to 20 which includes a plasmid pVgRxR.

22. A cell line as claimed in any of Claims 17 to 21 in which the cells are human embryonic kidney cells.

23. A cell line as claimed in Claim 22 in which the cells are EcR293 cells.

24. A cell line as claimed in any of Claims 17 to 20 in which the cells are natural β subunit-producing cells such as a HIBERNIA1 cell line.

25. A cell line having ECACC accession number 03112701.

26. A method of producing a cell line capable of producing a recombinant dimeric interleukin, or a subunit thereof, under transcriptional control of an ecdysone-inducible promoter, comprising the steps of:

- providing at least one expression vector according to any of Claims 1 to 11 or 16; and
- transfecting a host cell with the at least one expression vector,
- wherein the DNA encoding the at least one subunit of a dimeric interleukin is under the transcriptional control of an ecdysone-inducible mammalian expression system.

27. A method of preparing cDNA encoding a subunit of a dimeric form of interleukin comprising the steps of providing cDNA encoding the subunit, and digesting the cDNA with restriction enzymes *NheI* and *XhoI* to obtain a cDNA product.

28. A method of screening a candidate compound for the ability to inhibit dimer assembly and secretion of a dimeric form of interleukin, comprising the steps of:

- incubating a cell culture comprising a cell line of any of Claims 17 to 25 with the candidate compound;
- inducing transcription of the dimeric interleukin in the cells of the culture using ecdysone or an ecdysone analog; and
- assaying the cell culture for the presence of secreted interleukin.

29. A method as claimed in Claim 28, and in which the interleukin expressed by the cell line has a 6 x histidine amino acid sequence tagged on either or both of the subunits thereof, wherein the assaying step involves Ni-NTA affinity chromatography.

30. A method as claimed in Claim 28 in which the assaying step involves probing the cell culture with an antibody specific to a dimeric form of interleukin, or a subunit thereof.

31. An inhibitor of dimer assembly and secretion of dimeric interleukin identified by the method of any of Claims 28 to 30.

32. A method of prevention or treatment of inflammatory disease comprising a step of treating an individual with an inhibitor of Claim 31.

33. A method of treating disease having a pathogenesis which includes endogenous production of

any of cytokines IL-12, IL 23 or IL-27, the method comprising a step of treating an individual with an endoplasmic reticulum (ER) $Ca^{2+}$ perturbation reagent.

34. Use of an ER $Ca^{2+}$ perturbation reagent in the manufacture of a medicament for the treatment of disease having a pathogenesis which includes endogenous production of any of cytokines IL-12, IL-23 or IL-27.

35. Use of an ER $Ca^{2+}$ perturbation reagent for the treatment of disease having a pathogenesis which includes endogenous production of any of cytokines IL-12, IL-23 or IL-27.

36. A method of inhibiting the formation of one or more cytokines in an individual, which method comprises the step of treating an individual with ER $Ca^{2+}$ perturbation reagent.

37. Use of an ER $Ca^{2+}$ perturbation reagent to inhibit the formation of one or more cytokines in an individual.

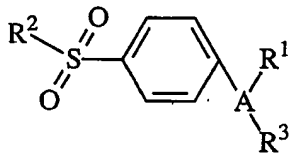
38. A method or use as claimed in any of Claims 33 to 37 in which the disease is an inflammatory disease in which one or more endogenously produced IL-12 forms play a disease promoting role.

39. A method or use as claimed in Claim 38 in which the IL-12 forms are αβ heterodimeric and ββ homodimeric forms.

40. A method or use as claimed in any of Claims 33 to 39 in which the disease is selected from the group consisting of infectious diseases; bacterial protozoal or virus-induced inflammation; epithelial airway inflammation such as asthma; allergic disease; autoimmune disease such as MS, RA and Inflammatory Bowel Disease; and -all conditions in which endogenously produced IL-12 α/β or ββ forms are thought to play a disease-promoting role.

41. A method or use as claimed in any of Claims 33 to 40 in which the ER $Ca^{2+}$ perturbation reagent is selected from the compounds of Formula I:

Formula I



wherein A is a substituent selected from partially unsaturated or unsaturated hetrocyclyl and partially unsaturated or unsaturated carbocyclic rings;
wherein $R^1$ is at least one substituent selected from hetercyclyl, cycloalkyl, cycloalkenyl and aryl,

wherein $R^1$ is optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

wherein $R^2$ is methyl or amino; and

wherein $R^3$ is a radical selected from hydrido, halo, alkyl, alkenyl, oxo, cyano, carboxyl, cyanoalkyl, heterocyclyloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclyl, cycloalkenyl, aralkyl, hetrocyclylalkyl, acyl, alkythioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalky, aryloxyalkyl, aralkylthioalky, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonalkyl, aminocarbonyl, aminocarbonylalkyl, alkyaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-arylamino, aminoalkly, alkylaminoalkyl, N-arylaminoalkyl, N-aralkylaminoalkyl, N-alkyl-N-aralkylaminoalky, N-alkyl-N-arylaminoalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-arylaminosulfonyl, arylsulfonyl, N-alkyl-N-arylaminosulfonyl; or a pharmaceutically-acceptable salt thereof.